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## **Blood pressure target attainment in the background of guidelines: the very elderly in Swiss primary care**

Schafer, H H ; Sudano, I ; Theus, G R ; Zilla, P ; Noll, G ; Burnier, M

**Abstract:** **BACKGROUND:** There are only a few trials for the very elderly population (>79 years). No consensus, which blood pressure (BP) goals and substances should be applied, has been found yet. This survey was undertaken to investigate how octogenarians are treated and attain BP targets in the Swiss primary care. **METHODS:** Data from 4594 hypertensive patients were collected within 7 days. Eight hundred and seventy-seven patients met the requirement to be >79 years. We assessed substances/combinations and investigated pulse pressure and target blood pressure attainment (TBPA) using three different recommendations [Canadian Hypertension Education Program (CHEP), Swiss Society of Hypertension (SSH), European Society of Hypertension-European Society of Cardiology (ESH-ESC)]. Secondly, we compared TBPA attained by angiotensin-converting enzyme inhibitor (ACEI)/diuretic (D), angiotensin receptor blocker (ARB)/D and calcium channel blocker (CCB)/D with any other dual therapy and investigated whether Ds/beta-blockers (BBs) or Ds/renin angiotensin-converting enzyme inhibitors (RAAS-Is) lead to higher TBPA. Finally, we assessed the impact of drug administration, practical work experience, location and specialization of GPs on TBPA. **RESULTS:** Octogenarians attained target blood pressure (TBP) between 44% (ESH-ESC) and 74% (SSH). Optimal/normal BP was reached in 22.8% of patients. Pulse pressure <65 mmHg was shown in 66.4% of patients. Monotherapy was most commonly applied followed by dual single-pill combination with ARB/D (46.5%) or ACEI/D (36.0%). No benefit in TBPA was found comparing a RAASI/D and CCB/D treatment with any other dual combination. There was also no difference between BB/D and RAAS-I/D combination therapy and between single-pill combination and dual free combinations. **CONCLUSIONS:** GPs adhere to the use of substances proven in outcome trials and attain high TBP. No difference in meeting BP goals could be found using different drug classes. There is an unmet need to harmonize recommendations and to add additional information for the treatment of octogenarians.

DOI: <https://doi.org/10.1093/fampra/cms012>

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ZORA URL: <https://doi.org/10.5167/uzh-63961>

Journal Article

Published Version

Originally published at:

Schafer, H H; Sudano, I; Theus, G R; Zilla, P; Noll, G; Burnier, M (2012). Blood pressure target attainment in the background of guidelines: the very elderly in Swiss primary care. *Family Practice*, 29(5):511-520.

DOI: <https://doi.org/10.1093/fampra/cms012>

# Blood pressure target attainment in the background of guidelines: the very elderly in Swiss primary care

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Received 12 July 2011; Revised 19 December 2011; Accepted 31 January 2012.

**Background.** There are only a few trials for the very elderly population (>79 years). No consensus, which blood pressure (BP) goals and substances should be applied, has been found yet. This survey was undertaken to investigate how octogenarians are treated and attain BP targets in the Swiss primary care.

**Methods.** Data from 4594 hypertensive patients were collected within 7 days. Eight hundred and seventy-seven patients met the requirement to be >79 years. We assessed substances/combinations and investigated pulse pressure and target blood pressure attainment (TBPA) using three different recommendations [Canadian Hypertension Education Program (CHEP), Swiss Society of Hypertension (SSH), European Society of Hypertension-European Society of Cardiology (ESH-ESC)]. Secondly, we compared TBPA attained by angiotensin-converting enzyme inhibitor (ACEI)/diuretic (D), angiotensin receptor blocker (ARB)/D and calcium channel blocker (CCB)/D with any other dual therapy and investigated whether Ds/beta-blockers (BBs) or Ds/renin angiotensin-converting enzyme inhibitors (RAAS-Is) lead to higher TBPA. Finally, we assessed the impact of drug administration, practical work experience, location and specialization of GPs on TBPA.

**Results.** Octogenarians attained target blood pressure (TBP) between 44% (ESH-ESC) and 74% (SSH). Optimal/normal BP was reached in 22.8% of patients. Pulse pressure <65 mmHg was shown in 66.4% of patients. Monotherapy was most commonly applied followed by dual single-pill combination with ARB/D (46.5%) or ACEI/D (36.0%). No benefit in TBPA was found comparing a RAASI/D and CCB/D treatment with any other dual combination. There was also no difference between BB/D and RAAS-I/D combination therapy and between single-pill combination and dual free combinations.

**Conclusions.** GPs adhere to the use of substances proven in outcome trials and attain high TBP. No difference in meeting BP goals could be found using different drug classes. There is an unmet need to harmonize recommendations and to add additional information for the treatment of octogenarians.

**Keywords.** Europe, guidelines, hypertension, octogenarians, Switzerland, target blood pressure attainment.

## Introduction

### *Hypertension in the very elderly*

Due to the increase of life expectation, cardiovascular late effects shift to high age. Although in 2050 approximately one-fifth of the 'older patients' will be >80 years and >60% of patients ≤65 years have hypertension, there are only a few trials that address this special population. Isolated systolic hypertension (ISH) occurs in a large number of older patients. Starting at the age of 60 years, systolic blood pressure (BP) is more related to neurovascular and cardiovascular events than the

diastolic BP. The National Health and Nutrition Examination Survey confirmed that 75% of patients did not reach their target blood pressure (TBP) because of a failure to accomplish systolic goals.<sup>1</sup>

### *Recommendations of guidelines*

Comprehensive treatment advice is lacking for the very elderly. Because no difference in the outcome by the use of certain substances could be shown<sup>2</sup> and the results of STOP-2<sup>3</sup> were indifferent, all substance classes are mentioned to be equally effective regardless of age. However, confirmation occurred for the

superiority of diuretics over beta-blockers (BBs) in reducing cardiovascular end points.<sup>4,5</sup> Recent data from the HYpertension in the Very Elderly Trial (HY-VET)<sup>6</sup> provided new evidence in favour of diuretics and angiotensin-converting enzyme inhibitors (ACEIs). Thus, this combination might currently constitute the optimal treatment approach (Table 2). For patients with ISH, VALUE<sup>7</sup> showed benefits for the combination calcium channel blocker (CCB)/diuretic. Therefore, according to ESH–ESC,<sup>8</sup> both substances are preferred for this special patient population.

Although in 2003<sup>9</sup> and 2007,<sup>8</sup> the ESH–ESC recommended to lower systolic BP <140 mmHg in patients ≥65 years, there was no advice for patients ≥79 years (octogenarians<sup>+</sup>). The results of HYVET<sup>6</sup> led to the change of the ESH–ESC reappraisal of 2009<sup>10</sup> with a new systolic BP goal of <150 mmHg. Different to this, the Canadian Hypertension Education Program (CHEP)<sup>4</sup> recommends to lower BP <140/90 mmHg for all patients irrespectively of the presence or absence of ISH and the Swiss Society of Hypertension (SSH)<sup>5</sup> applies BP goals <150/x mmHg. The recently published consensus document of the ACCF/AHA 2011<sup>11</sup> (Table 2) advises two treatment stratifications for patients ≥80 years with corresponding TBP. Pulse pressure >65 mmHg is strongly correlated with left ventricular hypertrophy and heart failure. Although pulse pressure calculation is helpful for risk stratification in patients >60 years, the ESH–ESC<sup>8</sup> does recommend BP measurement preferably to pulse pressure measurement for daily management.

#### *BP control and combination therapy*

Rates of BP control in primary care settings are reported to fall around 35%. Up to 75% of patients in the very elderly do not meet BP goals. As a result, the huge number of patients requires multidrug approaches to reach appropriate goals.<sup>12</sup> Combination therapy appears to have the potential to improve poor BP control and responder rates increase up to 70%<sup>13</sup> due to an increase of compliance and persistence.<sup>2</sup> Simplified formulations with high forgiveness factors<sup>14</sup> might be useful in octogenarians<sup>+</sup>.

#### *Aims of the survey*

Due to rising costs, a sufficient management of octogenarians<sup>+</sup> is essential and information about the quality of treatment in primary care has a high public interest. Because little data is available about the treatment of octogenarians<sup>+</sup> in Switzerland, the primary objectives of this survey were to investigate/identify

- the target pulse pressure- and TBP attainment (TBPA) according to the SSH,<sup>5</sup> ESH–ESC<sup>8</sup> and CHEP<sup>4</sup> (Table 2) guidelines,
- the amount of octogenarians<sup>+</sup> who may benefit by an intensified therapy approach (TBP <140 systolic according to ACCF/AHA 2011<sup>11</sup>),

- the most commonly prescribed substances and their combinations and
- differences in age-related prescribing behaviour of GPs and TBPA of patients with regards to GPs (i) subspecializations; (i) age and (iii) geographical location.

Secondarily, we investigated

- whether the combined therapy of ACEI/diuretics and angiotensin receptor blocker (ARB)/diuretics as well as CCB/diuretics is superior to any other dual therapy,
- whether diuretics combined with BBs or with a renin angiotensin-converting enzyme inhibitors (RAAS-Is) lead to higher TBPA and
- the impact of single-pill combination compared to dual free combination on TBPA.

## Materials and methods

For this survey, 450 GPs were chosen randomly from a list of all Swiss GPs and asked, in a letter, to include every adult patient (≥18 years) with diagnosed hypertension into the survey who visited the doctor's practice within 1 week. One hundred and fifty-seven GPs with different specializations responded to this call, performed by Healthworld Switzerland AG and submitted data of 4594 patients using a web database. The selection of GPs was performed on the basis of eight different postal code areas (Aargau, Basel, Bern/Oberwallis, Graubünden, Eastern-Switzerland, Western-Switzerland, Central-Switzerland/Tessin and Zurich/Thurgau) to ensure a representative statistic. GPs were assigned in two groups according to their specializations: (i) internal medicine and (ii) family medicine. Eight hundred and seventy-seven patients (23.6%) met the criteria to be treated and were of an age ≥80 years.

Demographic information (age, sex, weight and height), systolic/diastolic BP (assessed in sitting position with either auscultatory or oscillatory method), pulse pressure (>50, 50–64 and <64 mmHg) and heart rate were recorded. GPs were asked to report the presence of organ damage such as impaired renal function, stroke, heart failure, myocardial infarction (MI), atherosclerosis, left ventricular hypertrophy, microalbuminuria (30–300 mg/24 hours) and increase of serum creatinine (♂ up to 133 µmol/l and ♀ up to 124 µmol/l). Other clinical measurements were not required. Furthermore, we assessed risk factors including diabetes mellitus, pack years of nicotine abuse, dyslipidaemia [cholesterol >6.5 mmol/l, high-density lipoprotein (HDL) <1.0 mmol/l, LDL >4.0 mmol/l, triglyceride >1.7 mmol/l] and family history of cardiovascular disease. Laboratory values were processed when they were available (fasting glucose, total and HDL

cholesterol, potassium, creatinine, triglyceride, urea). For the documentation of the current therapy, substances or trademarks of both monotherapy and single-pill combination were selected interactively. Data of daily dosage and treatment duration were recorded using three time categories (<3, 3–6 and >6 months) and concomitant therapies could be mentioned (antidiabetic therapy, aspirin or lipid-lowering therapy) when applied. Patients were defined as diabetic if fasting glucose levels exceeded 7 mmol/l or if antidiabetic treatment was prescribed. GPs were asked to indicate the founding year of their practice which was assessed in three periods (1970–90, 1991–2000 and 2001–10) and used as an indirect marker for their age. Descriptive statistics (classical tests of hypotheses) were performed for the subgroup of patients  $\geq 80$  years using the software package R, version 2.12. Unpaired means were compared using *t*-test and one-way ANOVA followed by Bonferroni's correction if means of more than two groups were of interest. We compared dichotomous outcomes with chi-square test and compared ranks nonparametrically with either using the Mann–Whitney test or the Kruskal–Wallis test (with Dunn's post-test) for comparisons of more than two groups. Correlations were calculated with Pearson's moment correlation. Patients' characteristics for both groups (<80 and  $\geq 80$  years) were analysed for comparable reasons (Table 1). Due to the fact that the design of this survey did not meet the definition of a clinical study,<sup>15</sup> no ethic committee approval was necessary according to Swiss national law.<sup>16</sup> Nevertheless, the project was submitted to the ethical committee, Basel, for confirmation and clearance. The design of the questionnaire was created in cooperation with two members of the SSH in order to collect implementable information for future national recommendations and to provide adherence to wording and units for measurements used in the current SSH guidelines.

TABLE 1 Patients characteristics

	Patients $\geq 80$ years old ( <i>n</i> = 877)	Patients <80 years old ( <i>n</i> = 2843)
Sex: male/female (%)	36.4/63.6	54.4/45.6
Age (years)	84.8 ( $\pm 3.9$ )	63.8 ( $\pm 10.4$ )
Weight (kg)	70.8 ( $\pm 13.3$ )	81.8 ( $\pm 15.7$ )
Height (cm)	163.9 ( $\pm 8.7$ )	169.1 ( $\pm 8.8$ )
BMI (kg/m <sup>2</sup> )	26.3 ( $\pm 4.2$ )	28.6 ( $\pm 5.0$ )
BP		
Systolic BP (mmHg)	137.9 ( $\pm 16.4$ )	136.0 ( $\pm 13.8$ )
Diastolic BP (mmHg)	77.2 ( $\pm 10.1$ )	81.6 ( $\pm 8.8$ )
Heart rate (BPM)	73.3 ( $\pm 10.9$ )	73.0 ( $\pm 10.1$ )
Concomitant cardiovascular diseases		
MI (%)	13.3	10.2
Stroke (%)	14.1	4.7
Heart failure (%)	29.5	8.3

BMI, body mass index; BPM, beats per minute.

## Primary results

### Patients' characteristics

Octogenarians<sup>+</sup> showed more organ damages (71% versus 24.7%) than patients  $\leq 79$  years. One quarter of octogenarians<sup>+</sup> was detected with uncontrolled ISH, which represents an increase of 9.5% compared to patients  $\leq 79$  years. Octogenarians<sup>+</sup> were more likely to be affected by heart failure (29.5% versus 8.3%), stroke (14.1% versus 4.7%) and MI (29.5% versus 8.3%) than patients  $\leq 79$  years (Table 1). On the other hand, less patients were diagnosed with diabetes (–3.2%) and metabolic syndrome (–5.7%) in the subgroup of octogenarians<sup>+</sup>. The majority of octogenarians<sup>+</sup> appeared with Grade I hypertension or had high-normal BP. Patients (8.1%) were treated optimally and showed systolic/diastolic BP <120/80 mmHg. Patients (11.4%) suffered on Grades II or III hypertension (Fig. 1A). When comparing patients from urban and rural areas, there was no significant difference in age (*P* = 0.26), weight (*P* = 0.47) and body mass index (BMI) (*P* = 0.67). However, a tendency towards more MI (*P* = 0.009) and more strokes (*P* = 0.078) in rural areas could be suspected. Significantly, more patients living (*P* = 0.044) in the countryside were diagnosed with heart failure than in the Swiss cities.

### The distribution of pulse pressure and TBPA in the background of various guideline recommendations

In total, 33.5% of all patients showed an elevated pulse pressure >46 mmHg, while 18.8% had normal values (<50 mmHg). Applying the SSH guidelines (<150/90 mmHg), 74.1% of patients attained TBP (Fig. 1D) and 53.1% of patients reached the goals (<140/90 mmHg) of CHEP (Fig. 1B). In comparison, HYVET targets (<150/80 mmHg) were reached by only 44.2% of patients due to lower diastolic BP values (Fig. 1C). Applying TPB <130/80 mmHg for patients with renal impairment or diabetes mellitus, <150/90 mmHg for all octogenarians<sup>+</sup> with/without ISH resulted in a pooled TBPA of 57.2%. In total, 35.1% of all patients reached targets according to all three guidelines, while 25.9% did not meet a single goal provided in the investigated guidelines.

### Intensified treatment

According to the ACCF/AHA 2011<sup>11</sup> recommendation, 15.3% of octogenarians<sup>+</sup> attained TBP of 150/xx mmHg with one or two substances (Fig. 1E) irrespective of their admission as single-pill therapy or dual free combination. Therefore, these subjects qualified for intensified treatment (TBP <140/xx mmHg). In total, 21.9% of octogenarians<sup>+</sup> met BP goals of <150/xx mmHg with more than two substances.

**Distribution of applied substances and combinations.** In total, 85.9% of octogenarians<sup>+</sup> were actively treated.



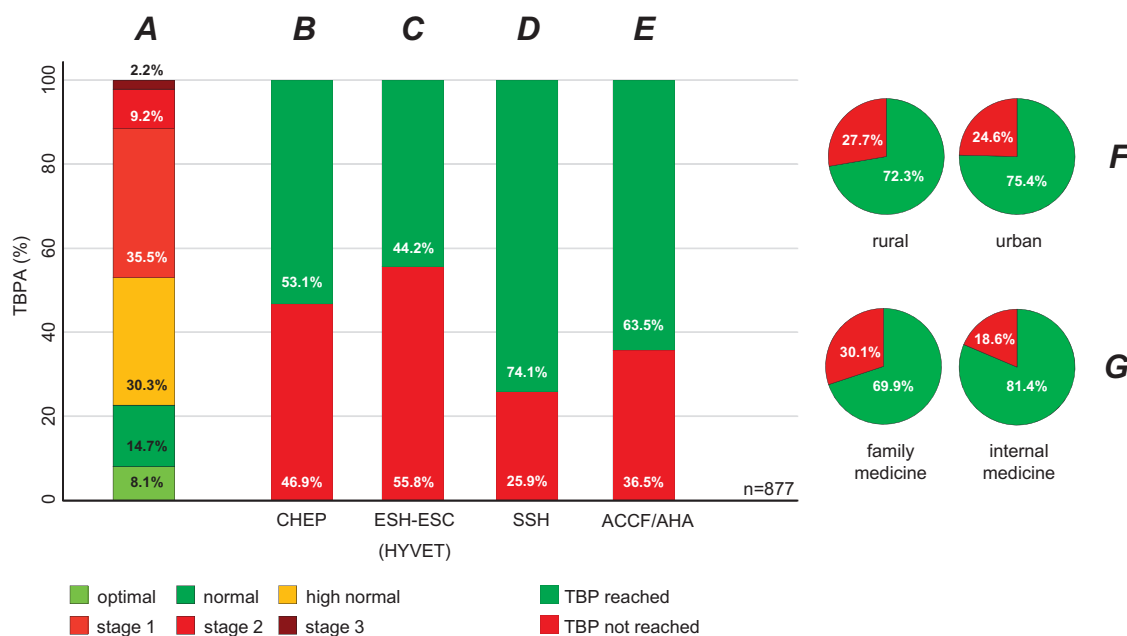


FIGURE 1 (A) Distribution of hypertension stages according to the guidelines of the SSH<sup>5</sup>—optimal (<120/180 mmHg), normal (120–129/80–84 mmHg), high normal (130–139/85–89 mmHg), Stage I (140–159/90–99 mmHg), Stage II (160–179/100–109 mmHg), Stage III ( $\geq 180/\geq 110$  mmHg), TBPA according to (B) CHEP,<sup>4</sup> (C) ESH-ESC,<sup>8</sup> (D) SSH,<sup>5</sup> (E) TBPA according to ACCF/AHA with one or two substances, (F) differences in TBPA<sub>SSH</sub> for urban and rural areas, (G) TBPA<sub>SSH</sub> according to subspecialization of GPs. SSH 2009, Swiss Society of Hypertension; ESC 2009, Reappraisal of European guidelines on hypertension management; CHEP, The 2010 Canadian Hypertension Education Program recommendations for the management of hypertension; ACCF/AHA 2011, Expert Consensus Document on Hypertension in the Elderly

Ninety-five per cent of all patients received a stable and unchanged regime of therapy for more than 6 months. Monotherapy was the most commonly used formulation (diuretics: 27.2%, ACEIs: 20.2%). Dual single-pill combination was administered with the second greatest frequency, for which diuretic-based regimes with ARBs (46.5%) and ACEIs (36.0%) were intensively chosen. The amount of prescribed ARBs in dual single-pill combinations increased (Fig. 3B) by 16.8% compared to dual free combination (Fig. 3A). The treatment approach using two single drugs was applied with the third greatest frequency in this survey. The most common combinations were BB/diuretics (25.3%) and ACEI/diuretics (15.6%). It is also remarkable that octogenarians<sup>+</sup> received a relatively high amount of BBs (39.4%).

Interestingly, in dual single-pill combinations, the amount of diuretics increased by 16.1% compared to dual free combination (Fig. 3A and B). Furthermore, there was a slight negative correlation for the use of ACEIs ( $r_{pb} = -0.11$ ) and ARBs ( $r_{pb} = -0.067$ ) by age, while for diuretics and BBs, no significant correlation could be calculated.

#### Impact of working years on prescribing behaviour and the influence of GPs' characteristics on TBPA

GPs who founded their practices between 2000 and 2009 prescribed the lowest amount of ARBs (−5.6%) and the highest amount of ACEIs (+3.9%) compared

to GPs who established their business between 1970 and 1989 (Fig. 2). The prescription of diuretics increased  $\sim 2.5\%$  during this period of time. We identified a slightly positive association between an earlier founding year of the practice and a higher responder rate to our survey. GPs in urban areas prescribed single-pill combinations more often ( $P = 0.003$ ) than GPs in rural areas of Switzerland. A similar tendency was observed when the specialization of the GPs was analysed. Thus, GPs with a speciality for internal medicine (GP<sub>int</sub>) recommended single-pill combinations more often ( $P = 0.009$ ) than their colleagues with a specialization for family medicine (GP<sub>fam</sub>), which was held by 60.2%. More than a half of all GPs were urbanely located (<10 000 inhabitants), while 45% worked in rural areas, where a lower density of GP<sub>int</sub> (23.3%) could be found (GP<sub>int</sub> in urban areas: 42.9%). Similarly, there were significantly more ( $P < 0.0001$ ) GP<sub>fam</sub> in rural areas. Our data show that there was no significant difference ( $P = 0.304$ ) in TBPA comparing GPs working in rural or urban areas (Fig. 1F).

A significant difference ( $P < 0.0001$ ) could be detected when comparing the speciality of GPs. GP<sub>int</sub> obtained in 81.36% TBP, meanwhile GP<sub>fam</sub> reached the goals for their patients in only 69.85% (Fig. 1G). This was supported by a significant difference of systolic BP ( $P < 0.0001$ ; GP<sub>int</sub> 134 mmHg, GP<sub>fam</sub> 139 mmHg). Patients' characteristics did not differ

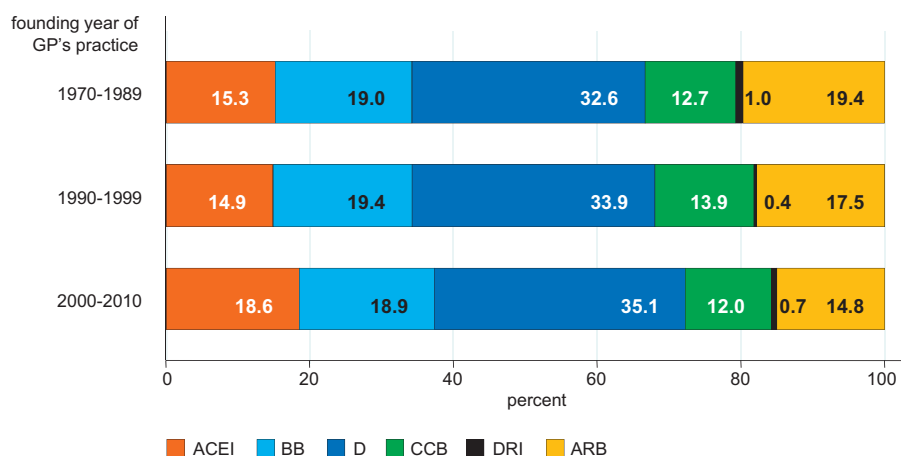


FIGURE 2 Doctor's experience and their therapies,  $n = 157$ ; CCB, calcium channel blocker; ARB, angiotensin receptor blocker; ACEI, angiotensin-converting enzyme inhibitor; BB, beta-blocker; D, diuretic; DRI, direct renin inhibitor

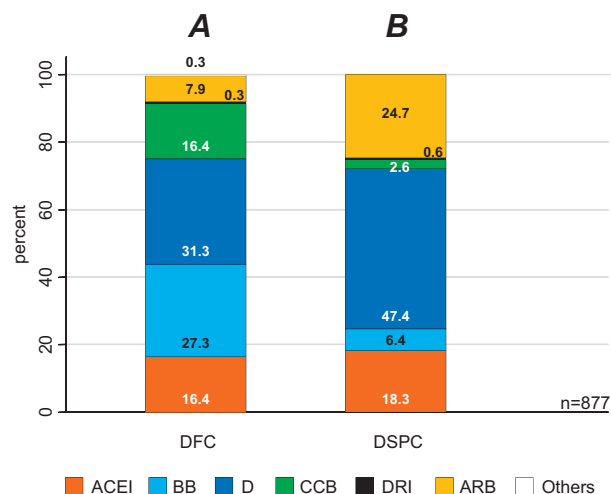


FIGURE 3 Distribution of substance classes used in DFC and DSPC. CCB, calcium channel blocker; ARB, angiotensin receptor blocker; ACEI, angiotensin-converting enzyme inhibitor; BB, beta-blocker; D, diuretic; DRI, direct renin inhibitor; DFC, dual free combination; DSPC, dual single-pill combination

significantly for age ( $P = 0.84$ ), weight ( $P = 0.40$ ) and BMI ( $P = 0.19$ ) when comparing  $GP_{fam}$  and  $GP_{fam-MI}$  ( $P = 0.79$ ), stroke ( $P = 0.079$ ) and heart failure (0.61) were similarly distributed within patients treated by GPs of both specializations. A slightly positive, though not significant, correlation could be detected between the age of GPs and TBPA.

## Secondary results

### *Influence of recommended combinations in TBPA according to SSH guidelines*

Neither a RAAS-I alone nor any recommended combination of this class with a diuretic led to a significant improved TBPA (ACEI/diuretic: 80.2%, ARB/diuretic:

73.6%) compared to other therapies. The use of CCBs alone and in combination with diuretics (75.2%) also had no impact in the same setting. Furthermore, there was no significant higher TBPA (76.8% versus 71.0%) between a diuretic-based combination with a RAAS-I (ACEI/diuretic, ARB/diuretic) and a diuretic-based combination with a BB.

### *The impact of single-pill combination on TBPA*

No difference in TBPA between single-pill combination therapy and dual free combination therapy in octogenarians<sup>+</sup> could be detected. Surprisingly, there was even a trend towards higher target attainments with dual free combination. Patients treated consecutively with dual free combinations showed a significantly lower systolic BP ( $P = 0.035$ ). Furthermore, a higher amount of patients with heart failure ( $P < 0.0001$ ), cardiac hypertrophy ( $P = 0.0009$ ) and chronic kidney disease ( $P = 0.0002$ ) received combined therapy with two separate pills.

## Discussion

Because there is no conclusive analysis in Switzerland that focuses on the treatment of the very elderly, this is the first big investigation that offers insight into how octogenarians<sup>+</sup> are managed in primary care. In addition, the problem of treatment quality according to specialization has never been addressed before for with this specific population.

Although the ESH-ESC 2007 stated clearly that the benefit of antihypertensive treatment is still unclear<sup>8</sup> and also in 2009,<sup>10</sup> no obligation for treatment was mentioned, our data show that 85.9% of octogenarians received treatment. This result reflects the awareness of GPs of changing evidence.

The difference (30%) between the ESH-ESC/HYVET and SSH is caused by a higher diastolic value

in the SSH guidelines, which is responsible for the increasing number of strokes and MI in the very elderly.<sup>17</sup> Although in this respect, ESH–ESC seems to be applicable, the Swiss recommendation (<150/x mmHg) reflects the fact that a systolic/diastolic BP of <140/80 mmHg (CHEP) is difficult to achieve in the very elderly. Furthermore, it was assumed after FRAMINGHAM<sup>18</sup> that impaired tissue perfusion in the elderly requires a slightly higher systolic BP.

Even though values of <140/90 mmHg lead to reduction of the cardiovascular risk in middle age patients, it must be mentioned that only one trial has been conducted with patients aged between 65 and 85 years that references this goal.<sup>19</sup> Until now, there are no studies that included octogenarians<sup>+</sup> with Stage I hypertension. As a result, the approach recommended by ACCF/AHA 2011<sup>11</sup> may be considered the most current and applicable one. Therefore, our data show that 15.3% of patients who reached TBP could benefit from

an intensified treatment by applying a TBP <140/xx mmHg (even though the treatment of octogenarians<sup>+</sup> in this survey was sufficient, according to SSH).

However, it should be noted that excessive lowering of the BP can reduce life quality and increases the cardiovascular risk. The International Verapamil - Trandolapril Study (INVEST) showed that drops of the diastolic target <65 mmHg led to a remarkable increase in mortality. Because treatment not only affects systolic BP and the diastolic value is often dependently linked, the ACCF/AHA 2011 considers a systolic range between 140 and 150/xx mmHg. Therefore, the unresolved problem remains that there is no recommendation for an appropriate diastolic value, although it is evident that both systolic and diastolic BPs have a similar impact on the incidence of strokes and coronary events.<sup>20</sup>

The high number of patients with ISH in octogenarians<sup>+</sup> (24.8%) in this survey is congruent with

TABLE 2 TBP and recommendations in different guidelines

	Age	ESH–ESC <sup>8</sup> 2007	ESH–ESC <sup>10</sup> 2009	CHEP <sup>4</sup> 2010	SSH <sup>5</sup> 2007/2008
Recommended TBP	≥65 Yrs		TBP ≤140/90 mmHg		
	≥80 Yrs	Not mentioned	TBP ≤150/xx mmHg if SBP was ≤160 mmHg initially	TBP ≤140/90 mmHg	Not mentioned
Recommended substances	≥65 Yrs	All substances (D, CCB, ARB, ACEI, BB)		All substances, no BB	All substances, especially D, no BB
	≥80 Yrs			Not mentioned	
Mentioned trials/substances applicable for the elderly/very elderly	≥65 Yrs			Not mentioned	
	≥80 Years	None	HYVET <sup>6</sup> (Indapamide/ACEI)		None
Treatment generally recommended?	≥65 Yrs			Yes	
	≥80 Yrs	Benefits of treatment unclear, continuation of treatment if well tolerated	Dependent on health condition, decision on individual base		Not mentioned
Advices for ISH (substances, TBP, trials)	≥65 Yrs	D, CCB	Not mentioned	D, ARB, CCB, TBP ≤140/90 mmHg	TBP ≤150/x mmHg
	≥80 Yrs			Not mentioned	
TBP applied in data analysis	≥80 Yrs independently of additional risk factors/organ damages:		<150/80 mmHg	<140/80 mmHg	<150/90 mmHg

ACCF/AHA 2011<sup>11</sup>

Recommended TBP: x – 79 yrs: <140/xx mmHg, 80 – x yrs: <140 – 150/xx, Exceptions for octogenarians: SBD <140 mmHg if TBP <150 mmHg can easily be obtained with one or two substances, SBD of <150 mmHg should be accepted if more than two substances are required, occurrence of unacceptable side effects or DBP <65 mmHg

ESH–ESC 2007, Guidelines for the Management of Arterial Hypertension; ESH–ESC 2009, Reappraisal of European guidelines on hypertension management; CHEP, The 2010 Canadian Hypertension Education Program recommendations for the management of hypertension; SSH 2009, Swiss Society of Hypertension; ACCF/AHA 2011, Expert Consensus Document on Hypertension in the Elderly; HYVET, HYpertension in the Very Elderly Trial; yrs, years; CCB, calcium channel blocker; ARB, angiotensin receptor blocker; ACEI, angiotensin-converting enzyme inhibitor; BB, beta-blocker; D, diuretic; DBP, diastolic blood pressure; SBP, systolic blood pressure.

TABLE 3 BP control, target organ damage and drug prescription according to the specialization of practitioners (family medicine, internal medicine) and to the location of the practitioners

	Family medicine (n = 534)	Internal medicine (n = 295)	P <sup>a</sup>	Rural area (n = 196)	Urban area (n = 593)	P <sup>a</sup>
Target BP <sub>SSH</sub> reached (%)	69.9	81.4	0.0003	72.3	75.4	0.30
SBP (mmHg)	139.7 (±17.4)	134.4 (±14.5)	<0.0001	137.9 (±16.3)	137.9 (±16.5)	0.96
DBP (mmHg)	77.5 (±10.2)	76.6 (±9.7)	0.21	77.4 (±10.4)	77.1 (±9.8)	0.67
MI (%)	13.9	13.2	0.79	11.1	14.9	0.09
Stroke (%)	15.7	11.5	0.09	16.6	12.4	0.08
Heart failure (%)	30.5	28.8	0.61	33.2	26.9	0.04
Atherosclerosis	52.9	54.9	0.59	49.9	55.0	0.13
Cardiac hypertrophy (%)	23.4	27.8	0.16	33.2	26.9	0.04
Microalbuminuria (%)	13.5	13.6	0.97	13.0	14.5	0.52
Smoking (%) <sup>b</sup>	10.3	13.9	0.12	9.7	12.6	0.18
Premature CVD family (%)	37.6	45.7	0.02	40.9	40.9	0.97
Diabetes (%)	23.0	21.0	0.5	22.7	22.5	0.93
CKD (%)	24.7	21.0	0.23	21.9	25.4	0.23
Age (years)	84.8 (±3.9)	84.9 (±3.9)	0.84	84.6 (±3.8)	84.9 (±3.9)	0.25
Sex (female) (%)	65.2	60.7	0.19	67.3	61.0	0.06
BMI (kg/m <sup>2</sup> )	26.4 (±4.2)	25.9 (±4.3)	0.21	26.3 (±4.0)	26.2 (±4.3)	0.65
Mono therapy (%)	29.6	30.1	0.78	28.5	29.8	0.67
DFC therapy (%) <sup>c</sup>	54.6	39.3	0.009	58.7	38.8	0.0003
SPC therapy (%) <sup>c</sup>	45.3	60.7	0.009	41.3	61.2	0.0003
Triple therapy (%)	23.2	21.4	0.54	23.3	22.7	0.84
BB (%)	41.0	36.3	0.18	40.7	38.6	0.52
D (%)	68.5	68.8	0.94	67.6	70.2	0.42
CCB (%)	28.8	23.4	0.09	27.7	26.6	0.71
ACEI (%)	33.3	28.5	0.15	35.2	30.0	0.11
ARB (%)	33.7	42.7	0.01	33.8	38.6	0.15
DRI (%)	1.7	0.7	0.34	1.1	1.6	0.77

CKD, chronic kidney disease; CVD, cardiovascular disease; D, diuretic; DFC, dual free combination; DRI, direct renin inhibitor; SPC, single-pill combination.

<sup>a</sup>P was calculated using chi-square test and *t*-test (SBP, DBP, age and BMI), respectively.

<sup>b</sup>Just actual smoking, we did not ask for smoking history.

<sup>c</sup>Quote of all patients treated with dual therapies (*n* = 326).

data from the Hypertension and Diabetes Risk Screening and Awareness trial.<sup>21</sup> This might be due to the fact that increased systolic BP values are often misinterpreted as physiologic in the primary care. Until now, there was a discrepancy among physicians on the application of cut-off levels in patients with ISH, as systolic BP of >160 mmHg has been previously classified as ISH and BP between 140 and 160 mmHg as borderline ISH. Since 2003, several studies applied systolic/diastolic BP cut-off levels >140/90 mmHg. The CHEP guidelines reflect this paradigm shift (Table 2), while the SSH recommends a slightly higher systolic goal (<150/x mmHg). To this day, there are still no 'general guidelines' for the treatment of hypertension in the very elderly. Although ACCF/AHA 2011 is a consensus document, it remains an 'expert document' that has not been implemented in national guidelines. The current situation appears with the following two problems:

- (1) Octogenarians<sup>+</sup> are only randomly mentioned, or they are included in the remarks about patients >65 years. The only guidelines that currently provide extended information are the ESC-ESH 2009

reappraisal<sup>10</sup> and the ACCF/AHA 2011. Goals applied in HYVET<sup>6</sup> are advised to be applicable in the very elderly; however, authors of the guidelines restrict their statements due to limited transferability of this trial to daily practice because most of the enrolled subjects were in good health without further co-morbidities, atypical for octogenarians<sup>+</sup>.

- (2) It is unclear how far additional risk factors must be reflected in the treatment and result in even lower TBP goals. We have shown the remarkable difference in TBPA when applying the cut-off level of 130/80 mmHg for high-risk patients. In the Cardio-Sis-study,<sup>22</sup> lower event rates were recorded with systolic TBP of <130 versus SBP <140 mmHg. In contrast, however, the results of Action to Control Cardiovascular Risk in Diabetes trial<sup>23</sup> yielded no difference in event rates when either a systolic BP of <120 or <140 mmHg was applied.

Pulse pressure increases continuously with age and leads to an increased cardiovascular risk. Therefore, a reduction of pulse pressure <65 mmHg is strongly



TABLE 4 Dual therapies: characteristics of octogenarians receiving either a single-pill combination or a dual free combination

	Single-pill combination (n = 172)	Dual free combination (n = 154)	P <sup>a</sup>
SBP (mmHg)	138.5 (±14.7)	135.2 (±15.4)	0.035
DBP (mmHg)	78.9 (±8.6)	76.4 (±10.1)	0.53
Target BP <sub>SSH</sub> achieved (%)	75.0	79.2	0.43
MI (%)	5.8	10.4	0.15
Stroke (%)	16.3	12.3	0.35
Heart failure (%)	13.9	37.7	<0.0001
Atherosclerosis (%)	43.0	57.8	0.01
Cardiac hypertrophy (%)	15.7	32.2	0.0009
Microalbuminuria (%)	8.7	14.3	0.12
Smoking (%) <sup>b</sup>	9.9	13.6	0.31
Premature CVD family (%)	39.5	42.2	0.65
Diabetes (%)	19.2	22.1	0.58
CKD (%)	12.8	26.6	0.002
Age (years)	83.9 (±3.5)	85.5 (±4.2)	0.0002
Sex (female) (%)	56.9	69.5	0.02
BMI (kg/m <sup>2</sup> )	26.2 (±4.2)	26.2 (±4.4)	0.96

CKD, chronic kidney disease; CVD, cardiovascular disease; D, diuretic; DRI, direct renin inhibitor; DFC, dual free combination; SPC, single-pill combination.

<sup>a</sup>P was calculated using chi-square test and *t*-test (SBP, DBP, age and BMI), respectively.

<sup>b</sup>Just smoking, we did not ask for smoking history.

recommended.<sup>2,8</sup> In this survey, 66.4% of all patients attained pulse pressure <65 mmHg, which is another indicator for a sufficient treatment of BP in Switzerland. Pulse pressure values are especially useful for the identification of patients with ISH although treatment according to SBP and DBP remains standard of care.<sup>24</sup>

In this survey, physicians mostly prescribed substances that are proven to be beneficial in outcome trials. Thus, RAAS-I and diuretics were used most frequently irrespective of the formulation, as the guidelines especially mention their gain in HYVET,<sup>6</sup> SCOPE<sup>25</sup> and LIVE.<sup>26</sup> Although Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial<sup>27</sup> provided evidence for diuretics in patients with hypertension, Avoiding Cardiovascular Events through Combination Therapy in Patients Living with Systolic Hypertension<sup>28</sup> showed that diuretic-based treatment led to more cardiovascular end points than CCBs in combination with ACEIs. The long-term use of diuretics was evident in nearly all combinations of this survey.

BBs were prescribed to a high extent, considering that SSH and CHEP guidelines do not recommend their use. It cannot be clarified if these substances were used exclusively for the treatment of hypertension or as secondary prevention of an MI. Also the amount of diuretics/BB combination (25.3%) in dual free combination remained high, although INVEST<sup>29</sup> provided evidence that the administration of a thiazide together with a BB led to an increase of cause-specific and cardiovascular events. ARBs/diuretics were chosen more often than ACEI/diuretics in dual single-pill

combination, which is in line with the fact that ARBs are prescribed in Switzerland preferentially to ACEIs. However, different to ACEIs, the administration of ARBs correlated negatively with the age of the patient and the founding year of the GP's practice. Higher tolerability of side effects in this life decade, less consultations of GP's and the habit to stick to long-term treatment are possible explanations for this tendency. Because of lower costs and high efficacy, younger GP's may consider a general adjustment of an ARB as unnecessary. Interestingly, diuretics/RAAS-Is were used more often in patients with uncontrolled ISH than CCB/diuretics, which is recommended by the ESH-ESC. This might be explained by MOSES,<sup>30</sup> which showed a lowering of stroke incidence by 25% when using an ARB instead of a CCB.

Our results show that GP<sub>int</sub> obtained significantly more often TBP compared to GP<sub>fam</sub>. This might be explained by the fact that GP<sub>fam</sub> often refer patients to other colleagues and specialists and maintain a managing role in Switzerland. This may lead to a situation of external and coexisting therapy plans that may have an impact on patient's compliance or result in the acceptance for higher BP due to a possible miscommunication. The distribution of prescription between GP<sub>int</sub> and GP<sub>fam</sub> indicates restraint in GP<sub>fam</sub> for single-pill combinations. Even though combined therapies can increase responder rates, it must be taken into consideration that a missed dose of a single-pill combination may have a higher impact on BP control than the non-adherence to one drug of a dual free combination. Considering that ~18% of octogenarians<sup>+</sup> suffer from cortical dementia, the risk of non-adherence to the prescribed medication is elevated. Furthermore, it must not be forgotten that the initial use of a single-pill combination can result in a substantial drop in BP. Therefore, it may be assumed that GP<sub>fam</sub> prefer a more steerable treatment approach which might be the result of low patient adherence to visits. In the other hand, GP<sub>int</sub> tend to prescribe a more simplified treatment regimen by the use of single-pill combination. However, our data showed that the TBPA between both administrations did not differ significantly.

### Limitations

This investigation was a cross-sectional analysis. Thus, we only detected uncontrolled ISH, and the actual number of patients might be higher. The lack of differences in TBPA in patients treated with RAAS-Is-CCB or diuretic-based combinations (Fig. 2E) compared to any other combinations might be caused by the fact that this survey was not designed to prove superiority of particular treatment regimes. As a result, the number of patients in the different groups was small and the statistical power insufficient. Physicians that participated in this survey might have had a higher interest in the treatment of arterial hypertension and thus may have

treated with higher success. Comparing the randomly chosen participants with regards to the postal codes, there was a slight over-representation of individuals from Basel and Graubünden. Physicians from Basel and Western-Switzerland included more patients than the other postal code areas. However, because there was no significant difference between responders and non-responders ( $P = 0.8$ ) in this survey with regards to the geographical location, a selection bias could be excluded. Despite these dissimilarities, there was also no significant difference ( $P = 9.7$ ) according to responders and non-responders with regards to their specialization. According to the Federal Office in Public Health,<sup>15,16</sup> study monitors are only allowed for clinical trials. As the current investigation is a survey, it could not be ensured that every patient who was visiting GPs practice was included. However, adherence to the procedure of this survey was maintained by a honorarium which was paid after inclusion of at least one patient per GP.

### Concluding remarks

Elderly patients are managed very efficiently in Swiss primary care. Up to 30.8% of patients reached optimal or normal BP and the actual number of treated patients was high (86%). Due to the strict adherence of Swiss physicians to the combinations used in outcome trials of elderly patients (D/ARBs, D/ACEIs), octogenarians<sup>+</sup> attained TBP between 44% and 74%. However, the amount of TBPA differed widely based on various guidelines. In the light of the compared guideline recommendations, approximately one quarter of octogenarians<sup>+</sup> require improvement in their treatment to reach TBP, while 15% of controlled patients could benefit from an intensified treatment with a BP goal <140/xx mmHg, according to SSH guidelines. Drug therapy can be generally considered useful, independent of patient's age, which may prevent cardiovascular events and contribute to a reduction of public health system costs.

### Acknowledgements

Luis Hoyos Restrepo, Harvard University, USA, Dorothy Daws, Chris Barnard Division of Cardiothoracic Surgery, University of Cape Town, Groote Schuur Hospital, Cape Town, South Africa and Oliver Hagan, Cape Town, South Africa.

### Declaration

Funding: the cross-sectional analysis was sponsored by an unrestricted grant from Novartis Pharma, Switzerland.

Ethical approval: none.

Conflict of interest: none.

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